

REMARKS

Applicants wish to thank Examiners Rooney and Haddad for discussing the present Office Action with Applicants' representative Angela Dallas Sebor during a telephonic interview conducted on January 31, 2008. The topics covered during the interview included the outstanding rejections under 35 U.S.C. § 112, first paragraph, and claims 36 and 37. The following remarks more fully capture the substance of the interview.

Status of the Claims

After this Amendment, claims 36-54 are now pending in the application. In the present Amendment, claims 36 and 53 have been amended and new claim 54 has been added. Support for these new and amended claims can be found throughout the specification and the originally filed claims. Applicants have not introduced any new matter by the amendments.

Specifically, support for a phosphoantigen that activates $\gamma\delta$ T cells can be found, *inter alia*, at page 31, lines 21-26, of the specification. Support for a mammal being a human can be found, *inter alia*, at page 40, lines 5-8, of the specification.

Clarification of Office Action Scope

Applicants note that the present Office Action apparently contains two separate examination reports, each beginning on a separate page 2: (1) a first, unsigned version containing a new matter rejection (¶ 4) and a written description rejection (¶ 5); and (2) a second, signed version containing the same new matter rejection (¶ 4), an enablement rejection (¶ 5), and the same written description rejection (¶ 6). It is Applicants' understanding that, as confirmed by the Examiner, all three rejections under

35 U.S.C. § 112, first paragraph, apply to the pending claims. Accordingly, Applicants address each basis of rejection below.

Rejections Under 35 U.S.C. § 112, First Paragraph

New Matter

Claims 36-53 were rejected under 35 U.S.C. § 112, first paragraph, as containing new matter not contained within the original specification. According to the Office, the content of claims 36-53 represents new matter for the reasons of record. Specifically, the Examiner contends that the specification “is directed to a method of identifying compounds that regulate airway hyperresponsiveness by modulating T cell action” and not “a method of reducing airway hyperresponsiveness using a phosphoantigen.” Office Action, page 6. The Examiner further asserts that the specification only mentions “phospho-antigen” and isoprenylpyrophosphate (IPP) as “possible compounds that can be identified in the disclosed method.” *Id.*

Applicants respectfully traverse. As discussed in the interview, the specification provides ample support for the use of phosphoantigens in the claimed methods. In broad terms, the specification clearly discloses the use of variety of agents (e.g., $\gamma\delta$ T cell agonists) that activate $\gamma\delta$ T cells and thereby reduce airway hyperresponsiveness in animals. The specification lists several groups of compounds that may act as $\gamma\delta$ T cell agonists and be used in the claimed methods. Among these groups of compounds are phosphoantigens, specific examples of which include IPP.

Applicants submit that one of skill in the art, upon reading the specification, would clearly recognize that phosphoantigens such as IPP are contemplated for use in reducing airway hyperresponsiveness. However, in the interest of clarity, the following

table provides the location of examples of support in the specification for the pending claims.

Claim Element	Example of Support in Specification
A method to reduce airway hyperresponsiveness in a mammal, comprising increasing $\gamma\delta$ T cell action in a mammal that has, or is at risk of developing, a respiratory condition associated with airway hyperresponsiveness	<p>"The present invention generally relates to a method to reduce or prevent airway hyperresponsiveness (AHR) in an animal that has, or is at risk of developing, airway hyperresponsiveness, by increasing the action of $\gamma\delta$ T cells (i.e., $\gamma\delta$ T lymphocytes) in the animal. In the method of the present invention, the animal has, or is at risk of developing, airway hyperresponsiveness associated with inflammation." Page 10, line 11-15.</p> <p>"In one embodiment, the method of the present invention includes the use of a variety of agents (i.e., regulatory compounds) which, by acting on $\gamma\delta$ T cells, increase the proliferation, activation/biological activity, and/or survival of $\gamma\delta$ T cells in the lung tissue of an animal, and/or the recruitment of other regulatory $\gamma\delta$ T cells to the lung tissue of the animal, such that airway hyperresponsiveness is reduced in the animal." Page 25, lines 5-9.</p>
administering a phosphoantigen that activates $\gamma\delta$ T cells to said mammal, wherein administration of said phosphoantigen reduces airway hyperresponsiveness in said mammal.	<p>"For the activation of $\gamma\delta$ T cells, the present invention also includes the use of 'phospho-antigens'." Page 31, lines 21-22.</p> <p>"In one embodiment, the method of the present invention includes the use of a variety of agents (i.e., regulatory compounds) which, by acting on $\gamma\delta$ T cells, increase the proliferation, activation/biological activity, and/or survival of $\gamma\delta$ T cells in the lung tissue of an animal, and/or the recruitment of other regulatory $\gamma\delta$ T cells to the lung tissue of the animal, such that airway hyperresponsiveness is reduced in the animal." Page 25, lines 5-9.</p>
wherein the phosphoantigen comprises isoprenylpyrophosphate (IPP).	"Phospho-antigens are antigens containing phosphate groups such as isoprenylpyrophosphate (IPP) and many others that have been characterized by the research groups of Michael Brenner and others (e.g., Tanaka et al., 1995, <i>Nature</i> 375:155-158)." Page 31, lines 22-24.

Claim Element	Example of Support in Specification
<p>wherein said phosphoantigen is administered so that the number of $\gamma\delta$ T cells in the lung tissue of said mammal increases.</p> <p>wherein said phosphoantigen is administered so that $\gamma\delta$ T cells in said mammal are activated.</p> <p>wherein said phosphoantigen is targeted to $\gamma\delta$ T cells in the lung tissue of said mammal.</p>	<p>"According to the present invention, the method for regulating airway hyperresponsiveness can be directed to any $\gamma\delta$ T cell, wherein an increase in the action of such $\gamma\delta$ T cell results in a decrease in airway hyperresponsiveness. Preferred $\gamma\delta$ T cells to activate and/or expand (i.e., proliferate, increase the numbers) are $\gamma\delta$ T cells in the lung tissue of an animal." Page 22, lines 3-7.</p>
wherein said phosphoantigen is targeted to $\gamma\delta$ T cells having a T cell receptor (TCR) selected from the group consisting of a murine TCR comprising Vy4 and a human TCR comprising V γ 1.	<p>"In one aspect, a preferred $\gamma\delta$ T cell for which increasing the action is believed to be particularly effective for reducing AHR has a T cell receptor (TCR) that comprises a Vy4 chain (i.e., the variable (V) region of the γ chain is has a particular sequence which is known in the art as Vy4, following the nomenclature of Tonegawa et al., for example), or the human equivalent thereof, which is believed to include Vδ1 T cells (i.e., Vy4 is the murine cell subset). Preferably, $\gamma\delta$ T cells having TCRs with Vy4 chains, or the human equivalent (e.g., Vδ1), are targeted by the method of the present method." Page 22, lines 16-22.</p>
wherein said phosphoantigen is administered by a route selected from the group consisting of inhaled, intratracheal and nasal routes.	<p>"Most preferably, an agent is administered to an animal by nasal, inhaled, or intratracheal routes." Page 33, lines 22-23.</p>
<p>wherein said phosphoantigen is administered to said mammal in an amount effective to reduce airway hyperresponsiveness in said mammal as compared to prior to administration of said phosphoantigen.</p> <p>wherein said phosphoantigen is administered with a pharmaceutically acceptable excipient.</p>	<p>"Preferably, the agent is administered to the animal in an amount effective to reduce airway hyperresponsiveness in the animal as compared to prior to administration of the agent. In one aspect, the agent is administered with a pharmaceutically acceptable excipient." Page 6, lines 21-24.</p>
<p>wherein said phosphoantigen is administered within between about 1 hour and 6 days of an initial diagnosis of airway hyperresponsiveness in said mammal.</p> <p>wherein said phosphoantigen is administered within less than about 72 hours of an initial diagnosis of airway hyperresponsiveness in said mammal.</p>	<p>"Without being bound by theory, the present inventors believe that the $\gamma\delta$ T cell responses which are effective to downregulate AHR are most effective within between about 1 hour to about 6 days after AHR is induced, and most preferably, within less than about 72 hours after AHR is induced." Page 24, lines 13-16.</p>
wherein said phosphoantigen is administered prior to development of airway hyperresponsiveness in said mammal.	<p>"In another embodiment, the $\gamma\delta$ T cell action is increased prior to development of airway hyperresponsiveness in the mammal." Page 6, line 28 to page 7, line 2.</p>

Claim Element	Example of Support in Specification
<p>wherein increasing $\gamma\delta$ T cell action by administration of said phosphoantigen decreases airway methacholine responsiveness in said mammal.</p> <p>wherein increasing $\gamma\delta$ T cell action by administration of said phosphoantigen improves said mammal's $PC_{20\text{methacholine}}\text{FEV}_1$ value such that the $PC_{20\text{methacholine}}\text{FEV}_1$ value obtained before increasing $\gamma\delta$ T cell action when the mammal is provoked with a first concentration of methacholine is substantially the same as the $PC_{20\text{methacholine}}\text{FEV}_1$ value obtained after increasing $\gamma\delta$ T cell action when the mammal is provoked with double the amount of the first concentration of methacholine.</p> <p>wherein said first concentration of methacholine is between about 0.01 mg/ml and about 8 mg/ml.</p>	<p>"In one embodiment, the method of the present invention decreases methacholine responsiveness in the animal. Preferably, the method of the present invention results in an improvement in a mammal's $PC_{20\text{methacholine}}\text{FEV}_1$ value such that the $PC_{20\text{methacholine}}\text{FEV}_1$ value obtained before use of the present method when the mammal is provoked with a first concentration of methacholine is the same as the $PC_{20\text{methacholine}}\text{FEV}_1$ value obtained after use of the present method when the mammal is provoked with double the amount of the first concentration of methacholine. Preferably, the method of the present invention results in an improvement in a mammal's $PC_{20\text{methacholine}}\text{FEV}_1$ value such that the $PC_{20\text{methacholine}}\text{FEV}_1$ value obtained before the use of the present method when the animal is provoked with between about 0.01 mg/ml to about 8 mg/ml of methacholine is the same as the $PC_{20\text{methacholine}}\text{FEV}_1$ value obtained after the use of the present method when the animal is provoked with between about 0.02 mg/ml to about 16 mg/ml of methacholine." Page 15, lines 10-21.</p>
<p>wherein increasing $\gamma\delta$ T cell action by administration of said phosphoantigen reduces airway hyperresponsiveness of said mammal such that the FEV_1 value of said mammal is improved by at least about 5%.</p>	<p>"In another embodiment, the method of the present invention improves an animal's FEV_1 by at least about 5%" Page 15, lines 22-23.</p>
<p>wherein said airway hyperresponsiveness is associated with a disease selected from the group consisting of chronic obstructive disease of the airways and asthma.</p>	<p>"Preferred conditions to treat using the method of the present invention include asthma, chronic obstructive disease of the airways, occupational asthma, exercise-induced asthma, pollution-induced asthma and reactive airway disease syndrome, with chronic obstructive disease of the airways and asthma being particularly preferred for treatment." Page 17, lines 6-10.</p>
<p>wherein the mammal is a human.</p>	<p>"Preferred mammals to treat using the method of the present invention include humans." Page 40, lines 7-8.</p>

As detailed in the above table, the specification provides clear support for the use of phosphoantigens, including IPP, for increasing $\gamma\delta$ T cell action in a mammal, thereby reducing airway hyperresponsiveness. Contrary to the Examiner's assertion,

phosphoantigens are not possible compounds that can be identified by screening methods disclosed in the application. Rather, the specification provides direct support for their use in reducing airway hyperresponsiveness, as recited in the instant claims.

In view of the specification's disclosure discussed above, one of skill in the art would immediately conclude that the inventors possessed the claimed invention and that the pending claims add no new matter to the application. Applicants thus request that these rejections be withdrawn.

Enablement

Claims 36-53 were also rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. Applicants respectfully traverse.

The pending claims recite methods to reduce airway hyperresponsiveness in a mammal comprising increasing $\gamma\delta$ T cell action in a mammal by administering a phosphoantigen that activates $\gamma\delta$ T cells to said mammal. According to the Office, the specification is enabling for methods to reduce airway hyperresponsiveness by administering TNF-alpha to a mammal, but not for carrying out the same methods by administering a phosphoantigen to a mammal. Office Action, page 12. The Examiner also contends that the recently submitted Declaration of Dr. Gelfand is not persuasive because the Declaration addresses the administration of TNF-alpha rather than phosphoantigens.

To satisfy the enablement requirement, the specification must contain sufficient disclosure to enable one skilled in the art to make and use the claimed invention without undue experimentation. M.P.E.P. § 2164. A determination of whether the claims are enabled thus involves, *inter alia*, the level of skill in the art and the amount of direction

provided by the inventor. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). Applicants submit that the specification provides sufficient disclosure to allow one of skill in the art to practice the full scope of the claims.

As an initial matter, the Gelfand Declaration not only presented results concerning the effect of TNF-alpha on airway hyperresponsiveness, but also demonstrated that $\gamma\delta$ T cells were required for the effect (e.g., TNF-alpha had no effect in $\gamma\delta$ depleted mice). Moreover, the results show that the deleterious effect of $\gamma\delta$ T cell depletion can be overcome by administering TNF-alpha to the mice. These results, taken together, suggest that TNF-alpha likely acts as a replacement for natural $\gamma\delta$ T cell cytokine secretion. Thus, one of skill in the art would clearly understand from these results that $\gamma\delta$ T cell activation plays a role in airway hyperresponsiveness, and agents that stimulate $\gamma\delta$ T cells to produce TNF-alpha would also be expected to reduce airway hyperresponsiveness.

In view of the arguments set forth in the Office Action, the Examiner's sole issue appears to be the contention that the specification does not teach one of skill in the art to substitute the administration of phosphoantigens for the administration of TNF-alpha in the claimed methods to reduce airway hyperresponsiveness. Applicants respectfully submit that the Examiner's contention is incorrect.

As elaborated in detail above, the specification expressly teaches methods to "reduce or prevent airway hyperresponsiveness (AHR) in an animal that has, or is at risk of developing, airway hyperresponsiveness, by increasing the action of $\gamma\delta$ T cells (i.e., $\gamma\delta$ T lymphocytes) in the animal." Specification, page 10, lines 11-14. The specification further teaches that a variety of agents can be used to induce the recited

increase in action of $\gamma\delta$ T cells.¹ *Id.* at page 25, lines 5-9. The Application then specifically teaches that phosphoantigens, including IPP, represent one group of agents that can be used to activate or increase the action of $\gamma\delta$ T cells. *Id.* at page 31, lines 21-24. The publication of Tanaka et al., which discloses the ability of IPP and a related family of prenyl pyrophosphate derivatives to activate $\gamma\delta$ T cells, is also referenced to provide examples of phosphoantigens suitable for use in the present invention. *Id.*

Considering the explicit teachings set forth above, it is clear that the specification expressly discloses the administration of phosphoantigens to increase the action of $\gamma\delta$ T cells in an animal and thereby reduce airway hyperresponsiveness. Applicants submit that the Examiner is requesting that each recitation of “agents” suitable for use in the claimed methods be accompanied by a list of all previously mentioned agents.

Satisfaction of the enablement requirement does not require such a rote recitation where the specification’s teachings are clear. What matters is that one of skill in the art, upon reading the disclosure of the instant application, would immediately recognize that phosphoantigens are “agents” that may be substituted for TNF-alpha in the methods of the invention to reduce airway hyperresponsiveness. Indeed, one need not be a skilled artisan to realize this aspect of the invention.

If the Examiner is asserting that the express teachings of the specification are inoperable, Applicants submit that it was known in the art, as of the priority date of the instant application, that phosphoantigens in general, and IPP in particular, were capable of activating $\gamma\delta$ T cells. As mentioned above, the publication of Tanaka et al.,

¹ “[T]he present invention includes the use of a variety of agents (i.e., regulatory compounds) which, by acting on $\gamma\delta$ T cells, increase the proliferation, activation/biological activity, and/or survival of $\gamma\delta$ T cells in the lung tissue of an animal, and/or the recruitment of other regulatory $\gamma\delta$ T cells to the lung tissue of the animal, such that airway hyperresponsiveness is reduced in the animal.”

referenced by the specification, discloses the activation of $\gamma\delta$ T cells by a family of phosphoantigens that includes IPP. The publication cited by the Examiner on page 18 of the Office Action (Burk et al., 1995) further demonstrates this principle. Burk et al. discloses six phosphoantigens, including IPP, that activate human $\gamma\delta$ T cells. These references establish that the skilled artisan was aware that phosphoantigens were capable of activating $\gamma\delta$ T cells as of the priority date of the present application.

Moreover, the references previously cited by the Examiner to demonstrate that the claimed invention is inoperable teach that the opposite is true. Sicard et al. concludes that administration of a phosphoantigen, BrHPP, represents a promising immunotherapeutic strategy for the induction of systemic Th1 cytokines and massive expansion of $\gamma\delta$ T cell subsets (see, for example, Abstract). Cendron et al. also concludes that phosphoantigen administration triggered immediate $\gamma\delta$ T cell activation and strong release of Th1 cytokines, while noting delayed responses to subsequent challenges in their model system (see page 561, col. 2).

Further, Applicants submit herewith the Declaration under 37 C.F.R. § 1.132 of Catherine Laplace as evidence that phosphoantigens can be used to reduce airway hyperresponsiveness in mammals according to the claimed methods. As set forth in the Declaration, three phosphoantigens, including IPP, BrHPP and a proprietary phosphoantigen termed “Compound X” activated human $\gamma\delta$ T cells and induced their production of TNF-alpha. These data are consistent with the art-recognized principle that phosphoantigens are capable of activating $\gamma\delta$ T cells.

The Declaration then describes an experiment assessing the effect of phosphoantigen treatment on early airway responses to inhaled allergen in rhesus

macaque monkeys. The results of this experiment indicate that when monkeys are treated with a phosphoantigen according to the methods of the present invention, a statistically significant reduction in airway hyperresponsiveness is observed. The results also suggest that, in a non-human primate model system, phosphoantigen treatment may lead to a commensurate reduction in airway hyperresponsiveness-related diseases such as COPD. Taken together, the experiments demonstrate that administering a phosphoantigen that activates $\gamma\delta$ T cells to a mammal reduces airway hyperresponsiveness in the mammal, as recited in the instant claims.

Compound X is a phosphoantigen and has a structure quite similar to IPP. In particular, both compound X and IPP contain two phosphate groups positioned on the same end of the molecule. Likewise, Compound X and IPP share a similar carbon backbone structure and both exhibit a low molecular weight. These shared structural characteristics are exactly the same as those known in the art to be essential for $\gamma\delta$ T cell-stimulating activity at the time of invention, as demonstrated by the teachings of Burk et al., the very publication cited by the Examiner to demonstrate the level of phosphoantigen knowledge in the art at this time. Post-filing publications further confirm the structure-function relationship disclosed in Burk et al.² Thus, the results presented in the Laplace Declaration demonstrate that administering a phosphoantigen with a core structure known in the art at the time of invention to activate $\gamma\delta$ T cells reduces airway hyperresponsiveness in a mammal, as recited in the instant claims.

² For example, the structure of Compound X is also similar to the general phosphoantigen structures set forth in Belmant et al (see Figure 1, correlating molecular structures of phosphoantigens with $\gamma\delta$ cell-stimulating bioactivities) and Espinosa et al (see Figure 1, showing structures of phosphorylated molecules that activate $\gamma\delta$ T cells).

Accordingly, in view of the evidence and remarks set forth above, Applicants submit that the specification is enabling for the full scope of the claimed methods to reduce airway hyperresponsiveness by administering a phosphoantigen to a mammal. Applicants thus respectfully request that all rejections under 35 U.S.C. § 112, first paragraph, for failure to comply with the enablement requirement be withdrawn.

Written Description

Claims 36-53 were also rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. According to the Office, the specification “does not adequately describe a genus of all phosphoantigen non-peptide compounds for use in the claimed invention.” Office Action, page 18. In essence, the Examiner contends that the specification does not provide structural data sufficient to distinguish phosphoantigens that would work to reduce airway hyperresponsiveness from those that would not work.

Applicants respectfully traverse these rejections. However, in an effort to clarify the invention and to expedite prosecution, Applicants have amended claims 36 and 53 to recite the administration of a phosphoantigen that activates $\gamma\delta$ T cells. Applicants submit that one of skill in the art, using the teachings of the instant specification and the knowledge in the art at the time of filing, would immediately understand that Applicants were in possession of the full scope of the claimed invention.

The written description requirement is satisfied if the specification discloses the invention in sufficient detail to allow a person skilled in the art to reasonably conclude that the inventor had possession of the invention as claimed. M.P.E.P. § 2163. While claims drawn to a genus may be adequately supported by the disclosure of a

representative number of species within the genus, the Federal Circuit has made clear that the specification need not describe every permutation of an invention nor subject matter known to those of skill in the art. *Capon v. Eshhar*, 418 F.3d 1349, 1359-60 (Fed. Cir. 2005). Moreover, an adequate written description of an invention that involves biological macromolecules need not contain a recitation of each known structure, particularly when those structures are already known in the art. *Falkner v. Inglis*, 448 F.3d 1357, 1366 (Fed. Cir. 2006) (“the forced recitation of known sequences in patent disclosures would only add unnecessary bulk to the specification. Accordingly, we hold that where . . . accessible literature sources clearly provided, as of the relevant date, [the sequences], satisfaction of the written description requirement does not require either the recitation or incorporation by reference”).

The claims, as amended, recite phosphoantigens that activate $\gamma\delta$ T cells rather than all known phosphoantigens. As previously discussed in the response to the Office Action dated May 3, 2007, the term phosphoantigen was well known to those of skill in the art at the time of the invention (see previously submitted references Belmant et al. and Espinosa et al.) These references, along with the publication of Tanaka et al., referenced by the specification, also establish that at the time of the invention, it was known that phosphoantigens could activate $\gamma\delta$ T cells.

Moreover, one of skill in the art also knew, at the time of invention, numerous examples of phosphoantigens capable of activating $\gamma\delta$ T cells, including detailed structural information on what aspects of the phosphoantigens contributed to the ability to activate the cells. Tanaka et al., for example, discloses a family of phosphoantigen compounds (prenyl pyrophosphate derivatives), including IPP, that activate $\gamma\delta$ T cells

and demonstrates structural aspects of these compounds that are responsible for the activation (see Abstract: “Substitution of phosphate for the pyrophosphate moiety, or elimination of the double bond, greatly reduced antigenic activity of the compounds.”) Similarly, Constant et al., *Science* 264:267-270 (1994), teaches a family of γ -derivatives of uridine triphosphate (X- γ UTP) and thymidine triphosphate (X- γ TTP) that activate $\gamma\delta$ T cells.

Additional evidence showing that the structural aspects of phosphoantigens that contribute to the activation of $\gamma\delta$ T cells was known in the art at the time of invention is provided by the teachings of Burk et al. The experiments and results described in Burk et al. provide detailed structural data on phosphoantigens that activate $\gamma\delta$ T cells, including the position of the phosphate moiety, the number and localization of the phosphate groups, the nature of the residues connected to the carbon backbone, and the molecular mass of the phosphoantigens.³ Indeed, the Examiner acknowledges these teachings by quoting Burk et al. to establish that “the art shows that ‘both the number and position of the phosphate groups, as well as the residues connected with the carbon backbone are required for stimulation’ of $\gamma\delta$ T cells.” Office Action, page 18. As with Tanaka et al. and Constant et al. discussed above, Burk et al. was published before the earliest priority date of the instant application.

Despite the Examiner’s recognition of the knowledge in the art, the Examiner contends that the specification fails to provide support for the pending claims because it does not provide the very structural features of phosphoantigens described in references

³ Burk et al. concludes, for example, “The position of the phosphate in the ligand is crucial”; “These data show that the number and the localization of the phosphate groups are critical for $\gamma\delta$ activation”; “we conclude that the nature of the residues connected with the carbon backbone determines their potency” and “the mass of the $\gamma\delta$ ligands is very small, resembling that of haptens.” Burk et al. at 2056-2057.

such as Burk et al. Applicants submit that the Examiner is improperly requiring that the specification include subject matter well known in the art and a description of each and every embodiment that may fall within the scope of the claims. Such a requirement is clearly contrary to what is needed to satisfy the written description requirement, as explained in the Federal Circuit's *Capon* and *Falkner* decisions.

Compliance with the written description requirement is assessed from the viewpoint of one skilled in the art, taking into account subject matter known in the field of invention. *S3, Inc. v. Nvidia Corp.*, 259 F.3d 1364, 1371 (Fed. Cir. 2001). Considering the knowledge in the art at the time of filing, in particular the knowledge of the activation of $\gamma\delta$ T cells by phosphoantigens having defined structural characteristics, one of skill in the art, upon reading the instant specification, would immediately understand that Applicants were in possession of the full scope of the claimed invention. To require the disclosure of material well known in the art at the time of the invention would serve only to add "unnecessary bulk" to the specification.

Accordingly, for at least the reasons discussed above, the specification provides enabling written description support for the full scope of the pending claims. Further, the pending claims have not added new matter to the application. Applicants thus request that all rejections under 35 U.S.C. § 112, first paragraph, be withdrawn.

Conclusions

In view of the foregoing amendments and remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims. If the Examiner has any questions regarding this Amendment and Response, the Examiner is invited to contact the undersigned at 303-863-9700.

The required small entity, one-month extension of time fee of \$60.00 is submitted herewith via EFS-Web. In the event that additional fees are due in connection with this response, please debit Deposit Account No. 19-1970.

Respectfully submitted,

SHERIDAN ROSS P.C.

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By: /John C. Stolpa/

John C. Stolpa
Registration No. 57,632
1560 Broadway, Suite 1200
Denver, CO 80202-5141
(303) 863-9700